REMARKS

Reconsideration is respectfully requested. Claims 20, 22, 23, and 30-39 are pending. Claims 1-19, 21 and 24-29 have been canceled. New claims 37-39 are added. Amendments to the claims do not add new matter and do not affect the inventorship.

Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections made by the Patent Office. Applicants reserve the right to pursue prosecution of any presently excluded claim embodiments in future continuation and/or divisional applications.

Claim Amendments

New claims 37 -39 are added. Support is found, for example, in page 13, lines 7-26, page 35, line 4, and page 34, line 30.

Claims Rejection - 35 U.S.C. § 112, First Paragraph

Claims 20, 22, 23, and 30-36 stand rejected under 35 U.S.C. 112,, first paragraph for alleged new matter. Applicants respectfully disagree.

Claims 20 and 30 require:

> a passivation agent monolayer comprising at least a covalently attached first passivation species and a covalently attached second passivation species comprising a protein binding ligand.

There is ample description in the specification. For example, the specification discloses a passivation agent monolayer at page 34, lines 10-19 ("the electrode further comprises a passivation agent, preferably in the form of a monolayer on the electrode surface"), that comprises two species, page 35, lines 28-29 ("The monolayer may comprise a single type of passivation agent, including insulators, or different types"), and page 37, lines 31-33 ("electrodes may be made that have any combination of components. Thus, a variety of different conductive oligomers or passivation agents may be used on a single electrode"), and page 34, lines 24-27 ("the passavation agents themselves may in fact be either (1) conducting or (2) nonconducting, i.e. insulating, molecules. Thus, in one embodiment, the passavation agents are conductive oligomers, as described herein, with or without a terminal group to block or decrease the transfer of charge to the electrode.")

The specification also discloses that the passivation agents are attached to the electrode covalently. See page 37, lines 16-18 ("a monolayer of passivation agents is added to the electrode.

Generally, the chemistry of addition is similar to or the same as the addition of conductive oligomers to the electrode, i.e. using a sulfur atom for attachment to a gold electrode, etc.")

The instant application also discloses passivation species comprising a protein binding ligand. See page 11, lines 8-10 ("when the analyte is a protein, the binding ligands include proteins (particularly including antibodies or fragments thereof (FAbs, etc.))"), page 20, lines 29-20 ("the binding ligand [is] attached, via a spacer, to the electrode"), page 21, line 8 ("the spacer is a conductive oligomer,") page 21, lines 5-6 ("the binding ligand may be attached via a non-conductive oligomer spacer.")

Therefore, contrary to the Examiner's contention, the specification has ample support for two different passivation species in the same monolayer. Accordingly, Applicants respectfully request the rejection be withdrawn.

Claims Rejection - 35 U.S.C. § 103

I. Claims 20, 30, 34 and 36

Claims 20, 30, 34 and 36 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Hollis et al. (WO 93/22678) ("*Hollis*") in view of *Agladze* (Metallurgy and Foundry Engineering (1997) 23(2), 127-137) ("*Agladze*")–Abstract only. Applicants respectfully traverse.

A. *Hollis*

The Examiner correctly notes that *Hollis* teaches microarrays and passivation layers. However, any similarity between *Hollis* and the instant invention ends there. For example, *Hollis* teaches a "glue" layer under a SiO_2 or Si_3N_4 passivation layers, which glue layer is exposed through discriminate ablation of the passivation layer. See, e.g., pg. 29, lines 5-7 and Figure 26. Thus, the net effect of ablation is elimination of the passivation layer at the point of ligand attachment—something *antithetical* to the merit of the instant claims, which are directed to a monolayer comprised of two passivation species, one of which is attached to a protein binding ligand.

The examiner incorrectly asserts that *Hollis* discloses "upper and lower electrodes covered with a film" at page 11, lines 14-32. *Hollis* does not disclose any film on the electrodes. The only "film" disclosed at this reference is a film of Si_3N_4 which is under the upper electrode.

The Examiner asserts that the apparatus of *Hollis* includes "a passivation agent monolayer." *Hollis* discloses a passivation layer which is not a monolayer. *Hollis* states "[t]he wells are passivated with a thin protective layer (not shown), such as silicon nitride or aluminum oxide to prevent degradation of the CCD device due to exposure to aqueous solution." Page 20, lines 16-19. On page 29, lines 13-16 *Hollis* states "[p]assivating materials can be hydrophobic materials such as fluorine-terminated

fluorocarbons or the derivatives or hexamethyldisilizane." There is no other description of a passivation layer in *Hollis*.

In the first example from *Hollis* the passivation layer is formed over a CCD device, not on measuring electrodes as in the present invention. Further, the "protection layer" of *Hollis* is composed of silicon nitride or aluminum oxide which are amorphous materials and are not monolayers.

In the second example from *Hollis*, the "passivating materials" are used to cover portions of a "glue" layer, not an electrode as in the present invention. Suggested materials are fluoramine-terminated fluorocarbons or the derivatives of hexadimethyldisilizane." Such passivating materials do not form monolayers over the glue layer.

As the Examiner correctly notes, *Hollis* describes a passivation layer on the electrodes at page 44, lines 6-9: "[a]lthough the method of detection will withstand some corrosion of the electrodes, a passivation layer can be employed to coat the plates for even longer use." However, this example of the use of a passivation layer is different the above where the layer coats a CCD device or a glue layer. *Hollis* does not indicate what this passivation layer is composed of and does not describe the use of a monolayer at any point in the patent application.

B. *Agladze*

As preliminary matter, Applicant notes that the examiner is relying on the abstract of the article. The abstract is not part of the full *Agladze* publication, but rather written by Chemical Abstract Service (CAS).

(1) *Agladze* is a non-analogous art

The Examiner cites *Agladze* for the proposition that "passivation films (layer) can modified [sic] electrode reactivity reactions via OH ions (species one) and anions (species two)." Applicant submits that *Agladze* is improperly cited as it is not analogous art.

"In order to rely on a reference as a basis for rejection of an applicant's invention, the reference must either be in the field of applicant's endeavor or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned." *In re Oetiker*, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992). M.P.E.P. §2141.01(a).

As for the former, the instant invention is directed to measuring electrodes comprising two passivation agent monolayer species, one of which comprises a protein binding ligand. In contrast, *Agladze* discusses studies in the field of metal corrosion. Specifically *Agladze* discussed the passivation of iron. Therefore, *Agladze* is not in the filed of applicant's endeavor.

As for the latter, the particular problem which the inventor was concerned is the efficiency of binding between the target analyte and the binding ligand, which would increase when the target analyte is at a distance from the electrode. Thus a "passivation agent layer facilitates the maintenance of the target analyte away from the surface of the electrode." Page 34, lines 11-14. In stark contrast, the concern of *Agladze*, as indicated by the tile, is about "The Modern Understanding of Corrosion and Passivation Process of Iron Group Metals." In *Agladze* the formation of passive film results in retardation of electrode reactions. See page 136, lines 23-24. Therefore *Agladze* is not reasonably pertinent to the particular problem with which the inventor was concerned - the efficiency of binding between the target analyte and the binding ligand.

For the forgoing reasons, *Agladze* is a non-analogous art and should not be cited.

(2) *Agladze* does not complement the deficiencies of *Hollis*.

Applicants further submit, contrary to the Examiner's assertion, *Agladze* does not disclose that the "OH ions and anions" form a monolayer.

The CAS abstract states that "...the formation of primary passive film consisting of adsorbed OH ions and anions results in a strong retardation of electrode reactions..." See also *Agladze*, page 136, lines 23-24. The Examiner makes the assumption that the OH ions and the anions are in the same monolayer. Contrary to the examiner's assumption, *Agladze* compares the differing affect of these different species and studies the species independently of one another. *Agladze* only provides the conjecture that "it is reasonable to assume that the primary passive film consists mainly of adsorbed hydroxide groups and anions adsorbed either according to solvent displacement or hydrogen-bonding mechanisms." Page 132, lines 22-24 (emphasis added). There is no teaching that the species are actually present at the same time. Thus, *Agladze* does not teach "that passivation films (layers) can modified [sic] electrode reactivity reactions via OH ions (species one) and anions (species two)."

Further, "OH ions and anions" do not form "monolayers" as they are taught in the instant application.

Moreover, claims of the present invention require that the passivation species of the monolayer be covalently attached. *Agladze* discloses "adsorbed OH ions and anions." The Examiner cites *Kaxiras*, another abstract, and states that "[t]he prior art shown that "adsorption" can produce covalent bonded passivation monolayers." There is no disclosure in *Agladze* that the anions and cations form bonds with the metal. In fact, *Agladze* teaches that the adsorbed species are not covalently attached but, rather, are held by physical forces that allow desorption: "The steady-state concentration of surface active sites in

this case will be determined by the balance of the rates of reactions of metal dissolution (1', 2'), adsorption and desorption of passivating film." Page 134, lines 29-31 (emphasis added).

(3) There is no motivation to combine *Agladze* with *Hollis* to reach the claimed invention

Agladze teaches corrosion prevention. A person of ordinary skill in the art of protein detection would not be motivated to search out techniques regarding corrosion prevention. See M.P.E.P. § 2141.01(a). Further, even assuming there was a proper motivation to combine the two references, it *still* would not result in the instantly claimed invention. *Hollis*' ligand layer overlaying an ablated glue layer assures that. Further still, for embodiments of the claimed invention in which the electrode is gold or platinum or graphite coated, it is difficult to see how iron corrosion is even remotely implicated.

Accordingly, Applicants respectfully seek reconsideration and withdrawal of this rejection, as the motivation to combine is completely lacking and the hypothetical combination still would not arrive at the claimed invention.

II. Claims 22, 23 and 31-33

Claims 22, 23 and 31-33 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over *Hollis* in view of *Agladze*, and further in view of Kayyem *et al.* US Patent No. 6,221,583 ("*Kayyem*") and Kossovsky *et al.* US Patent No. 5,585,646 ("*Kossovsky*"). The rejection is traversed as applied to Claims 22-23 and 31-33.

A. *Kayyem* is excluded under § 103 (c).

The Examiner has correctly quoted the relevant MPEP section, 706.2(l) and states that *Kayyem* is a 102(e) reference. However, the Examiner apparently fails to recognize the significance of that section, which further provides:

> The Cooperative Research and Technology Enhancement Act of 2004 (CREATE Act), in part, redesignated the former 35 U.S.C. 103(c) to 35 U.S.C. 103(c)(1) and made this provision ***effective to all applications in which the patent is granted on or after December 10, 2004***. Therefore, the provision of 35 U.S.C. 103(c)(1) is effective for all applications pending on or after December 10, 2004, including applications filed ***prior to*** November 29, 1999.
> M.P.E.P. 706.02(l)(1)(I). (Underscore and emphasis added).

The assignment records for the instant application and the *Kayyem* show common ownership in Clinical Micro Sensors (CMS). The instant application was filed on June 12, 1998. As of this January 2007, it *has yet to issue*. The '583 patent therefore falls within the plain

meaning of section 706.02(l)(1)(I) and, as such, Applicants are entitled to have it disqualified as prior art under 35 U.S.C. §103(c).

B. *Kossovsky*

For the reasons set forth previously, *Hollis* and *Agladze* combined do not render the claimed combinations obvious, and *Kayyem* is disqualified as a reference.

Further, *Kossovsky* does not overcome the deficiencies because *Kossovsky*, as the Examiner admits, is directed to polyhydroxide polysaccharide and carbohydrate passivation matrices, the end result of which would be an inability to limit ligand attachment to the external surface and thereby provide a discernable passivation layer separate from the ligand attachment site. As the Examiner notes, *Agladze* teaches the reactivity of polyhyroxides and the possibility for chemical modification thereof. Further, the instant claims contemplate two species of passivation layer, one of which is obligatorily bound to the ligand. *Kossovsky* does not teach or suggest this. Thus, once again, there is not proper motivation to combine the references, and *even combining them* does not result in the claimed invention. Accordingly, the Examiner is respectfully asked to reconsider and withdraw this ground of rejection.

III. Claim 35

Claim 35 stands rejected under 35 U.S.C. § 103 (a) as allegedly unpatentable over *Hollis*, in view of *Agladze* and further in view of *Wohlstadter et al.* US Patent No. 6,090,545 ("*Wohlstadter*"). The rejection is traversed as applied to claim 35.

For the reasons set forth previously, *Hollis* and *Agladze* combined do not render the claimed combinations obvious. *Wohlstadter* does not overcome these deficiencies. Accordingly, the Examiner has failed to make a prima facie case, and the references taken alone or combined cannot be said to anticipate or render obvious the claimed invention based on what the Examiner has articulated. For this reason, the instant rejection is respectfully asked to be reconsidered and withdrawn.

CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 442-1000.

Respectfully submitted,

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